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EXAMINER	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/588,558	SHORTIS, NICOLAS PETER	
	Examiner	Art Unit	
	Phyllis G. Spivack	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12-11-06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

An Information Disclosure Statement filed December 11, 2006 is acknowledged and has been reviewed.

Claims 1-13 are presented and represent all of the pending claims. The subject matter under consideration is entirely drawn to methods of treatment.

The disclosure is objected to for the following informalities: The acronyms "4ASA," "5ASA," "5-ASA," "4-ASA" and "4-ABA" in claims 7, 8, 11 and 13 should be spelled out the first time each is presented.

Appropriate correction is required.

The abstract of the disclosure is objected to because the Abstract should be presented on a separate sheet of paper without other parts of the application or other material. Correction is required. See MPEP § 608.01(b).

Claims 1-13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

The recitation "or other non-specific bowel disorder" in claims 1 and 11-13 renders the claims indefinite. The metes and bounds of those disorders contemplated cannot be precisely determined.

Clarification is required.

Claim 3 recites conditions (e.g., bloating, pain, cramping, distension, gas production) that characterize various non-inflammatory disease states (e.g., irritable bowel Syndrome, diverticulitis), as well as inflammatory intestinal disorders. Thus the claim lacks clarity.

Parenthetical subject matter in claim 7 renders the claim indefinite. It is unclear whether or not a claim limitation is intended.

Claims 12 and 13 provide for the use of balsalazide and 4-ASA or 5-ASA, respectively, but, since the claims do not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claims 12 and 13 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 1-13 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. This is a Written Description rejection.

Claims 1 and 11, respectively, recite “a derivative thereof” with respect to balsalazide and to a 4-ASA or 5-ASA compound modified to include a 4-ABA side chain or salt. There is insufficient written description for this claim limitation in the disclosure.

> M.P.E.P. § 2163 states, "An applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention...one must define a compound by 'whatever characteristics sufficiently distinguish it'. A lack of adequate written description issue also arises if the knowledge and level of skill in the art would not permit one skilled in the art to immediately envisage the product claimed from the disclosed process."

The term “derivative” encompasses a plethora of possible compounds. The specification fails to describe those derivatives contemplated and methods for their preparation. Such hypothetical compounds are not described in methods of treating non-inflammatory bowel diseases.

To provide adequate written description of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, structure/function correlation, methods of making the claimed compounds or any combination thereof. In the instant case, only a broad general statement directed to “derivatives” is provided. There is no description drawn to any methods wherein a specific therapeutic endpoint is achieved comprising administering a “derivative” of balsalazide or a “derivative” of a 4-ASA or 5-ASA compound modified to include a 4-ABA side chain.

Accordingly, it is not clear Applicant was in possession of the full scope of the claimed method at the time the invention was made. Adequate description requires more than a mere statement that derivatives are part of the invention. The skilled artisan could not "immediately envisage" the claimed derivatives based on the description provided in the disclosure.

Claim 1-13 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention. The claims are directed to the prophylaxis or treatment of any non-inflammatory bowel disease, diarrhea-predominant irritable bowel syndrome or other non-specific bowel disorder comprising administering balsalazide, optionally in combination with other therapeutic agents, or a 4-ASA or 5-ASA compound modified to include a 4-ABA side chain. In the context of the present claims, "prophylaxis" is taken to be synonymous with "prevention." The specification does not reasonably provide enablement for methods of prophylaxis within the full scope of the claims.

To be enabling, the specification must teach those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557, 1561 (Fed. Cir.1993). Explaining what is meant by "undue experimentation," the Federal Circuit has stated that:

> The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which

experimentation should proceed to enable the determination of how to practice a desired embodiment of the claimed invention. PPG v. Guardian, 75 F.3d 1558, 1564 (Fed. Cir. 1996).

The factors that may be considered in determining whether a disclosure would require undue experimentation are set forth by *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 wherein, citing *Ex parte Forman*, 230 USPQ 546 (Bd. Apls. 1986) at 547, the court recited eight factors to consider when assessing whether or not a disclosure would require undue experimentation. These factors are:

1) the quantity of experimentation necessary

2) the amount of direction or guidance provided

3) the presence or absence of working examples

4) the nature of the invention

5) the state of the art

6) the relative skill of those in the art

7) the predictability of the art and

8) the breadth of the claims.

These factors are always applied against the background understanding that scope of enablement varies inversely with the degree of unpredictability involved. *In re Fisher*, 57 CCPA 1099, 1108, 427 F.2d 833, 839, 166 USPQ 18, 24 (1970). Keeping that in mind, the Wands factors are relevant to the instant fact situation for the following reasons:

The nature of the invention, state of the prior art, relative skill of those in the art and the predictability of the art

The invention is drawn to the prophylaxis or treatment of any non-inflammatory bowel disease, diarrhea-predominant irritable bowel syndrome or other non-specific bowel disorders comprising administering balsalazide, optionally in combination with other therapeutic agents, or comprising administering a 4-ASA or 5-ASA compound modified to include a 4-ABA side chain. The relative skill of those in the art is high, generally that of an M.D. or Ph.D. with expertise in the area of gastroenterology.

However, that factor is outweighed by the unpredictable nature of the various pathologies that are encompassed in the recitations "non-inflammatory bowel disease" or "non-specific bowel disorder." In cases involving unpredictable factors, such as the instant claims drawn to physiological activity, the scope of enablement varies inversely with the degree of unpredictability of the factors involved. One skilled in the chemical or biological arts cannot always reasonably predict how different chemical compounds might behave under varying circumstances. See *Ex parte Sudilovsky* 21 USPQ2d 1701.

On pages 10-12 of the specification, testimonial Examples 1-3 are described wherein each of the three patients are suffering from either diarrhea-predominant irritable bowel syndrome or intermittent diarrhea/constipation irritable bowel syndrome. However, support for preventing any "non-inflammatory bowel disease" or any "non-specific bowel disorder" is absent. Clear support is provided only for irritable bowel syndrome. Accordingly, the disclosure is not commensurate in scope with the instant claims.

The present disclosure is clearly not predictable for prevention of any disorder. According to Borody, T.J., U.S. Patent 5,519,014, supplied by Applicant in the Information Disclosure Statement filed December 11, 2006, certain non-specific bowel disorders arise from unknown or non-obvious causes, which are unaccompanied by inflammation and are not due to detectable infection by known pathogenic organisms. See column 1, lines 10-15.

The amount of direction or guidance provided and the presence or absence of working examples

There are no working examples drawn to a prevention modality in which the claimed compounds are shown to be clinically effective for prevention of any non-inflammatory bowel disease or any non-specific bowel disorder. No guidance is provided drawn specifically to methods of prevention. Such an assertion is beyond the scope of the instantly claimed invention. The term "prevention" is an absolute definition that means to stop from occurring and thus requires a higher standard for enablement than does "therapeutic" or "treat". It is well established in the medical arts that the vast majority of diseases suffered by mankind cannot be totally prevented with current therapies.

The quantity of experimentation necessary

No direction is provided to distinguish therapy among the various disease states that are encompassed in the recitations "non-inflammatory bowel disease" and "non-specific bowel disorders." Absent reasonable *a priori* expectations of success for using a particular compound or derivative thereof, one skilled in the art would have to test

extensively many conditions to discover which compound elicits an effect in a treatment or prevention modality. Since each prospective embodiment, as well as future embodiments as the art progresses, would have to be empirically tested, undue experimentation would be required to practice the invention as it is claimed in its current scope. The specification provides inadequate guidance to do otherwise.

Prevention entails the complete and absolute inhibition of the onset of any non-specific bowel disorder or non-inflammatory bowel disease and any manifestation of the disease entirely.

Due to the known unpredictability of the art, and in the absence of experimental evidence commensurate in scope with the claims, the skilled artisan would not accept the assertion that any non-inflammatory bowel disease or non-specific bowel disorder could be prevented following the administration of any the claimed compounds. Accordingly, the instant claims do not comply with the enablement requirements of 35 U.S.C. 112, first paragraph, since to practice the claimed invention would require a person of ordinary skill in the art to engage in undue experimentation with no assurance of success.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422

F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claim 11 is rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 2, 4, 8 and 9 of U.S. Patent No. 5,519,014. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the patent are drawn to treating irritable bowel syndrome comprising administering a derivative of salicylic acid.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-10, 12 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wilson et al., WO 2005/030173.

Wilson teaches the administration of a colon-specific drug delivery system using interpolymer complexations of agents having a core of pharmaceutically active agent(s). See the Abstract. Those colon diseases encompassed by Wilson's teaching include irritable bowel syndrome (page 1, line 29). See the last paragraph on page 3, where **more than one active ingredient** may be employed. Among those active agents

contemplated are balsalazide, olsalazine, mesalamine (5-aminosalicylic acid), sulfasalazine, ipsalazide, the antibiotic metronidazole and anticholinergics. Also see claim 3, page 15.

Wilson provides motivation to treat irritable bowel syndrome with a reasonable expectation of success, using a colon-specific drug delivery system, wherein multiple active agents, such as balsalazide and an additional aminosalicylate, are formulated together and administered to a mammal.

Claims 11 is rejected under 35 U.S.C. 103(a) as being unpatentable over Wilson et al., WO 2005/030173, in view of Lin et al., U.S. Patent 6,326,364.

The teachings of Wilson are set forth *supra*.

Wilson fails to teach the administration of a 4-ASA or 5-ASA compound modified to include a 4-ABA side chain or a derivative thereof.

However, Lin teaches the administration of such derivatives that are conjugated dosage forms wherein, for example, a 5-aminosalicylic acid moiety, or a 5-amino salicylate moiety, is conjugated to another 5-amino aminosalicylic acid moiety or a 5-amino salicylate moiety. Balsalazide is specifically recited as a preferred conjugated 5-aminosalicylate compound. See column 8, lines 8-31. The administration may be to a human.

Therefore, in view of the combined teachings of Wilson and Lin, one skilled in the gastroenterology art would have been motivated to prepare a dosage form comprising a conjugate of a 4-ASA or 5-ASA compound modified to include a 4-ABA side chain or a derivative thereof for administration to a mammal to treat irritable bowel syndrome.

Such would have been obvious in the absence of evidence to the contrary because modification of aminosalicylates in the treatment of irritable bowel syndrome is disclosed by the combination of teachings of Wilson and Lin.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Phyllis G. Spivack whose telephone number is 571-272-0585. The Examiner can normally be reached on 10:30 AM-7 PM.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Ardin Marschel, may be reached on 591-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

April 27, 2008

/Phyllis G. Spivack/
Primary Examiner, Art Unit 1614